

1. A method for inducing prolonged *in vivo* gene expression in a mammal, comprising contacting a non-muscular tissue with a composition comprising a nucleic acid, a histone, and an amphipathic compound.

5 2. The method of claim 1, wherein said tissue is neuronal tissue.

3. The method of claim 1, wherein said tissue is a central nervous system (CNS) tissue

4. The method of claim 1, wherein said tissue comprises a post-mitotic neuronal cell.

10

5. The method of claim 1, wherein said tissue comprises a cortical neuronal cell.

6. The method of claim 1, wherein said tissue comprises a hippocampal neuronal cell, a glial cell, or a vascular endothelial cell.

15

7. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least 48 hours after contacting said tissue with said composition.

20

8. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least 72 hours after contacting said tissue with said composition.

9. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least 96 hours after contacting said tissue with said composition.

25

10. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least one week after contacting said tissue with said composition.

11. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least two weeks after contacting said tissue with said composition.

30

12. The method of claim 1, wherein gene expression in said tissue is detected *in vivo* for at least four weeks after contacting said tissue with said composition.

13. The method of claim 1, wherein said composition is in the form of a liposome.

14. The method of claim 13, wherein said liposome is neutral or cationic

5 15. The method of claim 13, wherein said liposome is anionic.

16. The method of claim 1, wherein said histone is selected from the group consisting of H1, H2A, H2B, H3, and H4.

10 17. The method of claim 1, wherein said composition further comprises a nuclear localizing signal.

18. The method of claim 1 wherein the amphipathic compound is a non-natural polyamine having a hydrophobic moiety, said polyamine being selected from the group consisting of a C6-C24 alkane, C6-C24 alkene, sterol, steroid, lipid, fatty acid, and hydrophobic hormone.

15 19. The method of claim 1, wherein said nucleic acid is an AD7c-NTP antisense molecule or a nitric oxide synthase III antisense molecule.

20 20. The method of claim 19, wherein said nucleic acid comprises a sequence complementary to the nucleotide sequence of SEQ ID NO:1.

25 21. A non-transgenic model for Alzheimer' Disease, comprising a non-human animal, wherein said animal comprises an exogenous AD7c-NTP nucleic acid.

22. The model of claim 21, wherein said non-human animal expresses an exogenous AD7c-NTP polypeptide in a neuronal cell of said animal for at least 48 hours.

30 23. The model of claim 21, wherein said animal is a rodent.

24. The model of claim 21, wherein said animal is a non-human primate.

25. The model of claim 22, wherein said neuronal cell is selected from the group consisting of a cortical neuronal cell, a hippocampal neuronal cell, a cerebellar neuronal cell, and a glial cell.

5

26. The model of claim 21, wherein said non-human animal expresses an exogenous AD7c-NTP polypeptide in a vascular endothelial cell of said animal.

10 27. A non-transgenic model for Alzheimer' Disease, comprising a non-human animal, wherein said animal comprises a exogenous nitric oxide synthase nucleic acid.

28. The model of claim 27, wherein said nucleic acid encodes a nitric oxide synthase III polypeptide.

15 29. The model of claim 27, wherein said non-human animal expresses an exogenous nitric oxide synthase polypeptide in a neuronal cell of said animal for at least 48 hours.

30. The model of claim 27, wherein said non-human animal expresses an exogenous nitric oxide synthase polypeptide in a neuronal cell of said animal for at least 72 hours.

20

31. The model of claim 27, wherein said non-human animal expresses an exogenous nitric oxide synthase polypeptide in a neuronal cell of said animal for at least 2 weeks.

25 32. The model of claim 27, wherein said non-human animal expresses an exogenous nitric oxide synthase polypeptide in a neuronal cell of said animal for at least 4 weeks.

33. A method of inhibiting Alzheimer's Disease-associated neuronal cell death, comprising contacting an AD7c-NTP-overexpressing cell with a composition comprising an

30 AD7c-NTP antisense nucleic acid and a histone polypeptide,

34. The method of claim 33, wherein said composition further comprises an amphipathic compound.

35. A method of inhibiting Alzheimer's Disease-associated neuronal cell death, comprising contacting an AD7c-NTP-overexpressing cell with an inhibitor of insulin or insulin-like growth factor-1 dependent signal transduction.

36. The method of claim 35, wherein said inhibitor is a composition which binds to residues 2-14 of SEQ ID NO:2.

37. The method of claim 35, wherein said composition comprises an antibody, antibody fragment, polypeptide, or organic molecule.

38. The method of claim 35, wherein said inhibitor is administered at a dose which inhibits apoptosis.

39. A method of inhibiting Alzheimer's Disease-associated neuronal cell death, comprising contacting an AD7c-NTP-overexpressing cell with an inhibitor of an IRS-dependent growth factor.

40. The method of claim 39, wherein said growth factor is insulin like growth factor-1 (IGF-1).

41. The method of claim 39, wherein said growth factor is insulin.

42. The method of claim 39, wherein said inhibitor binds to an N-terminal insulin/IGF1 receptor domain in AD7c-NTP.

43. The method of claim 39, wherein said inhibitor is an antibody, antibody fragment, polypeptide, or organic molecule.

44. A method of inhibiting Alzheimer's Disease-associated neuronal cell death, comprising contacting an Adc7-NTP-overexpressing cell with an inhibitor of nitric oxide synthase III.

5 45. A method of inhibiting Alzheimer's Disease-associated neuronal cell death, comprising contacting an Adc7-NTP-overexpressing cell with an inhibitor of insulin.

46. A method of identifying a compound which inhibits Alzheimer's Disease-associated neuronal cell death, comprising contacting an AD7c-NTP over-expressing cell with a 10 candidate compound and measuring cell viability, wherein an increase in cell viability in the presence of the compound compared to in its absence indicates that said compound inhibits Alzheimer's Disease associated neuronal cell death.

15 47. The method of claim 46, wherein said cell is a primary cerebellar neuronal cell.

48. The method of claim 46, wherein said cell comprises an exogenous AD7c-NTP encoding DNA.

20 49. The method of claim 46, wherein said cell expresses an exogenous AD7c-NTP polypeptide in an inducible manner.

50. A method of identifying a compound which inhibits Alzheimer's Disease-associated neuronal cell death, comprising contacting a non-human animal expressing a heterologous AD7c-NTP nucleic acid in a neuronal tissue of said animal, with a candidate compound and 25 measuring neuronal cell viability, wherein an increase in cell viability in the presence of the compound compared to in its absence indicates that said compound inhibits Alzheimer's Disease associated neuronal cell death.

30 51. A method of identifying a compound which inhibits a symptom of Alzheimer's Disease, comprising contacting a non-human animal expressing a heterologous AD7c-NTP nucleic acid in a neuronal tissue of said animal, with a candidate compound and detecting amyloid precursor protein (APP) expression in said tissue, wherein an decrease in APP

expression in the presence of the compound compared to in its absence indicates that said compound inhibits a symptom of Alzheimer's Disease.

52. A method of identifying a compound which inhibits a symptom of Alzheimer's  
5 Disease, comprising contacting a non-human animal expressing a heterologous AD7c-NTP nucleic acid in a neuronal tissue of said animal, with a candidate compound and detecting amyloid plaques in said tissue, wherein an decrease in the amount of said plaques in the presence of the compound compared to in its absence indicates that said compound inhibits a symptom of Alzheimer's Disease.

10

10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400 410 420 430 440 450 460 470 480 490 500 510 520 530 540 550 560 570 580 590 600 610 620 630 640 650 660 670 680 690 700 710 720 730 740 750 760 770 780 790 800 810 820 830 840 850 860 870 880 890 900 910 920 930 940 950 960 970 980 990 1000